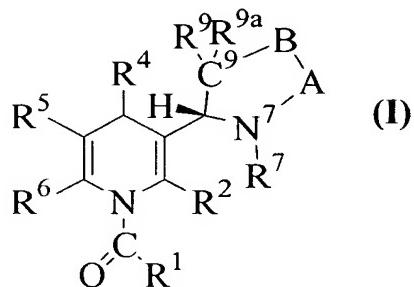


THAT WHICH IS CLAIMED IS:

1. A method of making a compound of **Formula I**:



wherein:

R⁴ is alkyl, alkenyl, alkynyl, aryl or SiR²⁰R²¹R²², wherein R²⁰, R²¹ and R²² are each independently selected from the group consisting of alkyl, alkenyl, alkynyl and aryl;

R¹ is alkyl, aryl, alkenyl, alkynyl, alkoxy, -NR"₂ or -SR", where R" is alkyl, aryl, alkenyl, alkynyl, or alkoxy;

R², R⁵, and R⁶ are each independently selected from the group consisting of H, alkyl, aryl, alkenyl, alkynyl, alkoxy, and halo;

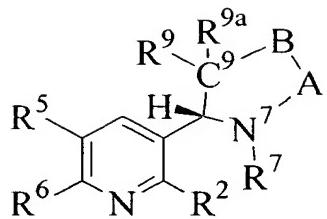
R⁷ is selected from the group consisting of H and alkyl;

A is a 1, 2 or 3 atom bridging species which forms part of a saturated or monounsaturated 5-, 6- or 7-membered ring including N⁷, C⁸, C⁹ and B;

B is selected from -O-, -S-, -NR¹⁰-, wherein R¹⁰ is selected from hydrogen, alkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl, substituted arylalkyl; -C¹⁰HR^{10a}-, wherein R^{10a} is selected from hydrogen, alkyl, hydroxyalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, --OR', -NR'₂, or --SR', wherein each R' is independently hydrogen, alkyl, alkenyl, alkynyl or aryl; or B is =C¹⁰R^{10a} or =N-; and

R⁹ and R^{9a} are each independently selected from hydrogen, alkyl, hydroxyalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, -OR', -NR'₂, or -SR', wherein each R' is as defined above;

comprising reacting an organometallic nucleophile R⁴Met, where R⁴ is as given above and Met is a metal, with a compound of the formula:



wherein A, B, R², R⁵, R⁶, R⁷, R⁹, and R^{9a} are as given above,

and a compound of the formula R¹COX¹, wherein R¹ is as given above and X¹ is halo, to produce a compound of **Formula I**.

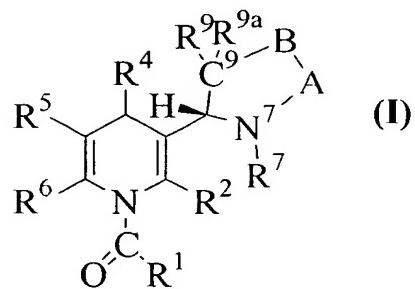
2. The method of claim 1, wherein R⁴ is alkyl, alkenyl, alkynyl, or aryl.

3. The method of claim 1, wherein R⁴ is SiR²⁰R²¹R²², and wherein R²⁰, R²¹ and R²² are each independently selected from the group consisting of alkyl, alkenyl, alkynyl and aryl.

4. The method of claim 1, wherein R¹ is alkyl.

5. The method of claim 1, wherein Met is selected from the group consisting of magnesium, manganese, sodium, lithium, copper, cerium, zinc, cadmium, aluminum and titanium.

6. A compound of **Formula I**:



wherein:

R⁴ is alkyl, alkenyl, alkynyl, aryl or SiR²⁰R²¹R²², wherein R²⁰, R²¹ and R²² are each independently selected from the group consisting of alkyl, alkenyl, alkynyl and aryl;

R¹ is alkyl, aryl, alkenyl, alkynyl, alkoxy, -NR"₂ or -SR", where R" is alkyl, aryl, alkenyl, alkynyl, or alkoxy;

R², R⁵, and R⁶ are each independently selected from the group consisting of H, alkyl, aryl, alkenyl, alkynyl, alkoxy, and halo;

R⁷ is selected from the group consisting of H and alkyl;

A is a 1, 2 or 3 atom bridging species which forms part of a saturated or monounsaturated 5-, 6- or 7-membered ring including N⁷, C⁸, C⁹ and B;

B is selected from -O-, -S-, -NR¹⁰-, wherein R¹⁰ is selected from hydrogen, alkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl, substituted arylalkyl; -C¹⁰HR^{10a}-, wherein R^{10a} is selected from hydrogen, alkyl, hydroxyalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, --OR', -NR'₂, or --SR', wherein each R' is independently hydrogen, alkyl, alkenyl, alkynyl or aryl; or B is =C¹⁰R^{10a} or =N-; and

R⁹ and R^{9a} are each independently selected from hydrogen, alkyl, hydroxyalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, -OR', -NR'₂, or -SR', wherein each R' is as defined above.

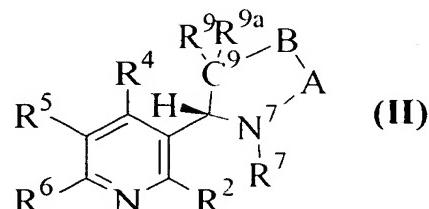
7. The compound of claim 6, wherein R⁴ is alkyl, alkenyl, alkynyl, or aryl.

8. The compound of claim 6, wherein R⁴ is SiR²⁰R²¹R²², and wherein R²⁰, R²¹ and R²² are each independently selected from the group consisting of alkyl, alkenyl, alkynyl and aryl.

9. The compound of claim 6, wherein R¹ is alkyl.

10. The compound of claim 6, wherein said compound is enantiomerically pure.

11. A method of making a compound of **Formula II**:



wherein:

R^4 is alkyl, alkenyl, alkynyl, aryl or $SiR^{20}R^{21}R^{22}$, wherein R^{20} , R^{21} and R^{22} are each independently selected from the group consisting of alkyl, alkenyl, alkynyl and aryl;

R^2 , R^5 , and R^6 are each independently selected from the group consisting of H, alkyl, aryl, alkenyl, alkynyl, alkoxy, and halo;

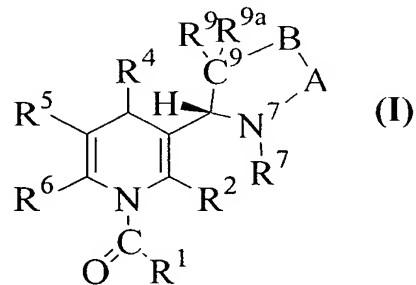
R^7 is selected from the group consisting of H and alkyl;

A is a 1, 2 or 3 atom bridging species which forms part of a saturated or monounsaturated 5-, 6- or 7-membered ring including N^7 , C^8 , C^9 and B;

B is selected from -O-, -S-, -NR¹⁰-, wherein R¹⁰ is selected from hydrogen, alkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl, substituted arylalkyl; -C¹⁰HR^{10a}-, wherein R^{10a} is selected from hydrogen, alkyl, hydroxyalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, --OR', -NR'₂, or --SR', wherein each R' is independently hydrogen, alkyl, alkenyl, alkynyl or aryl; or B is =C¹⁰R^{10a} or =N-; and

R^9 and R^{9a} are each independently selected from hydrogen, alkyl, hydroxyalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, -OR', -NR'₂, or -SR', wherein each R' is as defined above;

comprising oxidizing a compound of **Formula I**:



wherein A, B, R^2 , R^4 , R^5 , R^6 , R^7 , R^9 , and R^{9a} are as given above, and R^1 is alkyl, aryl, alkenyl, alkynyl, alkoxy, -NR"₂ or -SR", where R" is alkyl, aryl, alkenyl, alkynyl, or alkoxy, to produce a compound of **Formula II**.

12. The method of claim 11, wherein said solvent is toluene.

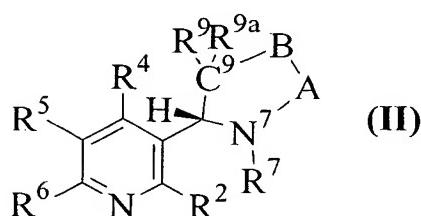
13. The method of claim 11, wherein said oxidizing step is carried out with an oxidizing agent selected from the group consisting of air, sulfur, nitric acid, KMnO₄, ceric ammonium nitrate, chloranil and 2,3-dichloro-5, 6-dicyano-1, 4-benzoquinone.

14. The method of claim 11, wherein R^4 is alkyl, alkenyl, alkynyl, or aryl.

15. The method of claim 11, wherein R^4 is $SiR^{20}R^{21}R^{22}$, and wherein R^{20} , R^{21} and R^{22} are each independently selected from the group consisting of alkyl alkenyl, alkynyl and aryl.

16. An enantiomerically pure C4-substituted nicotine analog produced by the process of claim 11.

17. An enantiomerically pure compound of **Formula II**:



wherein:

R^4 is alkyl, alkenyl, alkynyl, aryl or $SiR^{20}R^{21}R^{22}$, wherein R^{20} , R^{21} and R^{22} are each independently selected from the group consisting of alkyl alkenyl, alkynyl and aryl;

R^2 , R^5 , and R^6 are each independently selected from the group consisting of H, alkyl, aryl, alkenyl, alkynyl, alkoxy, and halo;

subject to the proviso that R^4 is different from at least one of R^2 , R^5 and R^6 ;

R^7 is selected from the group consisting of H and alkyl;

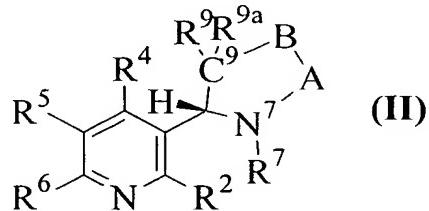
A is a 1, 2 or 3 atom bridging species which forms part of a saturated or monounsaturated 5-, 6- or 7-membered ring including N⁷, C⁸, C⁹ and B;

B is selected from -O-, -S-, -NR¹⁰-, wherein R¹⁰ is selected from hydrogen, alkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl, substituted arylalkyl; -C¹⁰HR^{10a}-, wherein R^{10a} is selected from hydrogen, alkyl, hydroxylalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, --OR', -NR'₂, or --SR', wherein each R' is independently hydrogen, alkyl, alkenyl, alkynyl or aryl; or B is =C¹⁰R^{10a} or =N-; and

R^9 and R^{9a} are each independently selected from hydrogen, alkyl, hydroxylalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, -OR', -NR'₂, or -SR'. wherein each R' is as defined above.

18. The enantiomerically pure compound of claim 17, subject to the proviso that R⁴ is different from R², R⁵ and R⁶.

19. An enantiomerically pure compound of **Formula II**:



wherein:

R⁴ is SiR²⁰R²¹R²², wherein R²⁰, R²¹ and R²² are each independently selected from the group consisting of alkyl, alkenyl, alkynyl and aryl;

R², R⁵, and R⁶ are each independently selected from the group consisting of H, alkyl, aryl, alkenyl, alkynyl, alkoxy, and halo;

R⁷ is selected from the group consisting of H and alkyl;

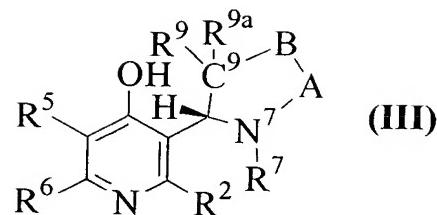
A is a 1, 2 or 3 atom bridging species which forms part of a saturated or monounsaturated 5-, 6- or 7-membered ring including N⁷, C⁸, C⁹ and B;

B is selected from -O-, -S-, -NR¹⁰-, wherein R¹⁰ is selected from hydrogen, alkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl, substituted arylalkyl; -C¹⁰HR^{10a}-, wherein R^{10a} is selected from hydrogen, alkyl, hydroxyalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, --OR', -NR'₂, or --SR', wherein each R' is independently hydrogen, alkyl, alkenyl, alkynyl or aryl; or B is =C¹⁰R^{10a} or =N-; and

R⁹ and R^{9a} are each independently selected from hydrogen, alkyl, hydroxyalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, -OR', -NR'₂, or -SR', wherein each R' is as defined above.

20. The compound of claim 19, wherein R², R⁵, and R⁶ are each independently selected from the group consisting of H, alkyl, aryl, alkenyl, and alkynyl.

21. A method of making a compound of **Formula III**:



wherein:

R^2 , R^5 , and R^6 are each independently selected from the group consisting of H, alkyl, aryl, alkenyl, alkynyl, alkoxy, and halo;

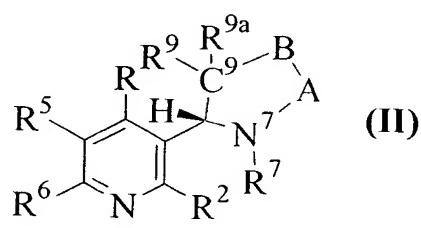
R^7 is selected from the group consisting of H and alkyl;

A is a 1, 2 or 3 atom bridging species which forms part of a saturated or monounsaturated 5-, 6- or 7-membered ring including N^7 , C^8 , C^9 and B ;

B is selected from $-O-$, $-S-$, $-NR^{10}-$, wherein R^{10} is selected from hydrogen, alkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl, substituted arylalkyl; $-C^{10}HR^{10a}-$, wherein R^{10a} is selected from hydrogen, alkyl, hydroxylalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, $--OR'$, $-NR'_2$, or $--SR'$, wherein each R' is independently hydrogen, alkyl, alkenyl, alkynyl or aryl; or B is $=C^{10}R^{10a}$ or $=N-$; and

R^9 and R^{9a} are each independently selected from hydrogen, alkyl, hydroxylalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, $-OR'$, $-NR'_2$, or $-SR'$, wherein each R' is as defined above;

comprising oxidizing a compound of **Formula II**:

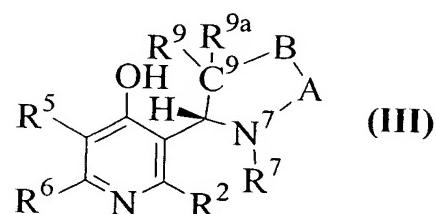


wherein A , B , R , R^2 , R^5 , R^6 , R^7 , R^9 , and R^{9a} are as given above and R is $SiR^{20}R^{21}R^{22}$, wherein R^{20} , R^{21} and R^{22} are each independently selected from the group consisting of alkyl, alkenyl, alkynyl and aryl, in a polar protic solvent to produce a compound of **Formula III**.

22. The method of claim 21, wherein said solvent is selected from the group consisting of methanol, ethanol, propanol, and butanol.

23. The method of claim 21, wherein said oxidizing step is carried out with a peroxide in the presence of fluoride.

24. An enantiomerically pure compound of **Formula III**:



wherein:

R², R⁵, and R⁶ are each independently selected from the group consisting of H, alkyl, aryl, alkenyl, alkynyl, alkoxy, and halo;

R⁷ is selected from the group consisting of H and alkyl;

A is a 1, 2 or 3 atom bridging species which forms part of a saturated or monounsaturated 5-, 6- or 7-membered ring including N⁷, C⁸, C⁹ and B;

B is selected from -O-, -S-, -NR¹⁰-, where R¹⁰ is selected from hydrogen, alkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl, substituted arylalkyl; -C¹⁰HR^{10a}-, where R^{10a} is selected from hydrogen, alkyl, hydroxyalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, --OR', -NR'₂, or --SR', wherein each R' is independently hydrogen, alkyl, alkenyl, alkynyl or aryl; or B is =C¹⁰R^{10a} or =N-; and

R⁹ and R^{9a} are each independently selected from hydrogen, alkyl, hydroxyalkyl, aryl, aryloxyalkyl, fluoro, trifluoromethyl, cyano, cyanomethyl, -OR', -NR'₂, or -SR', wherein each R' is as defined above.